REMARKS

Upon entry of the foregoing amendment, claims 14, 16-20, and 28 are pending in the application, with 14 being the independent claim. Claim 20 has been withdrawn by the Examiner. Claim 17 has been amended. Support for the amendment to claim 17 is found in the specification at page 14, lines 13-15. New claim 28 has been added. Support for claim 28 is found in the specification at page 3, lines 4-6. These changes are believed to introduce no new matter, and their entry is respectfully requested.

Based on the above amendment and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

Rejections Under 35 U.S.C. § 112

Claim 17 has been rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement. (Office Action, page 2). Applicants respectfully traverse this rejection.

The Examiner alleges that the claim is not enabled for the full scope of inducing a prophylactic immune response to prevent bacterial, viral, fungal, and parasitic infections and cancer. (Office Action, page 3). The Examiner is further of the opinion that the claim is reasonably interpreted to encompass the entry of a single microorganism into a cell of a host and that Applicants have not demonstrated that this can be prevented using the present invention. (Office Action, page 4).

Applicants respectfully disagree. Claim 17 as amended is directed to a method of inducing an immune response comprising concurrently administering an immunogen and compound 48/80 to a subject in an amount effective to produce an immune response therein, wherein said immunogen and said compound 48/80 are administered simultaneously in a common pharmaceutical carrier, wherein the immune response is a prophylactic immune response to bacterial or viral infection. Applicants assert that the claim is fully enabled over its entire scope. Methods of raising prophylactic immune responses to bacterial or viral

infections are well known in the art. There are numerous examples in the art of standard and well known prophylactic vaccines to various bacterial and viral diseases, including chickenpox, diphtheria, tetanus, pertussis, *Haemophilus influenzae* type b, hepatitis A, hepatitis B, influenza, measles, mumps, rubella, pneumococcus, polio, rotavirus, and anthrax, as disclosed on page 12 of the present specification. One of skill in the art at the time the present application was filed was familiar with all of these successful examples and with the techniques and materials required to induce a prophylactic immune response.

In light of the advanced level of knowledge in the art regarding methods of generating prophylactic immune responses, it is not necessary for Applicants to provide detailed guidance or working examples in order to enable claim 17. "The specification need not explicitly teach those in the art how to make and use the invention; the [enablement] requirement is satisfied if, given what they already know, the specification teaches those in the art enough that they can make and use the invention without 'undue experimentation.'" *See Amgen Inc. v. Hoechst Marion Roussel Inc.*, 65 USPQ2d 1385, 1400 (Fed. Cir. 2003). The present specification provides sufficient detail to enable one of skill in the art how to carry out the invention in view of what was already known in the art at the time of filing. The specification discloses viral and bacterial organisms that may be targeted and immunogens that may be used (page 8, line 25 to page 13, line 2), dosages of immunogen and Compound 48/80 that can be used (page 13, line 23 to page 14, line 6), suitable co-adjuvants (page 15, line 10 to page 16, line 11), and routes and means of administration (page 16, line 12 to page 19, line 22). This level of direction and guidance, in view of the knowledge in the art, is more than adequate to enable the full scope of claim 17.

As further evidence of the enablement of claim 17, Applicants provide a Declaration under 37 C.F.R. 132 of Dr. Herman Ford Staats, one of the inventors listed on the present application. The Declaration describes experiments carried out using methods disclosed in the specification, demonstrating that that claimed methods of raising an immune response are effective to provide a prophylactic immune response against exposure to vaccinia virus. Dr. Staats further states that he expects similar prophylactic immune responses to be induced when Compound 48/80 is used as an adjuvant with immunogens from other microorganisms.

Thus, the Declaration provides experimental evidence that the present specification provides sufficient support for the enablement of claim 17.

Applicants disagree with the Examiner's opinion that claim 17 is not enabled based on the interpretation of the claim as encompassing the prevention of entry of one microorganism into host cells. First, the Examiner has not presented any evidence to show that the claimed method would not be expected to prevent the entry of a single organism into a host cell. In order to establish a *prima facie* case of lack of enablement, the Examiner has the initial burden to set forth a reasonable basis to question the enablement provided for the claimed invention. *See In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). To satisfy this burden, "it is incumbent upon the Patent Office. . . to explain *why* it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement." *See In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971) (emphasis in original). In the absence of evidence provided by the Examiner showing that the claimed method would not be expected to prevent the entry of a single organism into a host cell, Applicants are not required to prove that the claimed invention does function to prevent the entry of a single microorganism into a host cell.

Second, the Examiner is incorrect in stating that a prophylactic immune response requires the prevention of entry of a single microorganism into a cell. A prophylactic immune response against a microorganism is one that prevents a subject from becoming infected with that microorganism. The method by which the immune response functions to prevent infection is irrelevant to the enablement of the present claim. Whether the prophylactic immune response kills a microorganism in an extracellular space, prevents a microorganism from entering a cell, kills a microorganism after it enters a cell, prevents a microorganism from traveling from one cell to another, or all of the above, it is still a prophylactic immune response. Applicants are not required to disclose the mechanism by which an invention works in order to enable the invention. They are only required teach one of skill in the art how to carry out the invention without undue experimentation. The present specification does so.

Moreover, the presence of inoperative embodiments within the scope of a claim does not necessarily render a claim nonenabled. The standard is whether a skilled person could determine which embodiments that were conceived, but not yet made, would be inoperative or operative with expenditure of no more effort than is normally required in the art. MPEP § 2164.08(b). Here, one of skill in the art could determine if a particular immunogen, together with Compound 48/80, induces a prophylactic immune response using simple and routine experiments involving administering the composition to a subject, exposing the subject to a microorganism, and determining if an infection occurs. Thus, Applicants have clearly enabled the full scope of claim 17.

Applicants respectfully request that the rejection of claim 17 under 35 U.S.C. § 112, first paragraph be withdrawn.

Rejections Under 35 U.S.C. § 103

Claims 14 and 16-19 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Rosok *et al.* (U.S. Patent No. 4,834,976) in view of Lenney *et al.* (*J. Pharm. Sci. 66*:702 (1997)). (Office Action, page 6). Applicants respectfully traverse this rejection.

The Examiner alleges that Rosok *et al.* teach a composition comprising an immunogen and antimicrobial agent with a pharmaceutical carrier, pointing to Claim 17. (Office Action, page 7). The Examiner states that Rosok *et al.* do not teach the use of Compound 48/80 as an antimicrobial agent, that Lenney *et al.* teach the antimicrobial properties of Compound 48/80, and that it would have been obvious to use Compound 48/80 as the antimicrobial agent in the composition of Rosok *et al.* (Office Action, page 8.)

Applicants respectfully disagree. Rosok *et al.* do not teach a composition comprising an immunogen and an antimicrobial agent. The entire disclosure of Rosok *et al.* is directed to monoclonal antibodies that recognize the flagella of *Pseudomonas aeruginosa* and the use of the antibodies for treatment or prophylaxis of *P. aeruginosa* infection (column 4, lines 14-38). Nowhere in Rosok *et al.* is it taught or suggested to administer an immunogen to a host to raise a therapeutic or prophylactic immune response to the immunogen. The only use of an

immunogen described in Rosok *et al.* is the delivery of an immunogen to an animal for the purpose of generating monoclonal antibodies. Claim 17 in Rosok *et al.* is directed to a pharmaceutical composition comprising a monoclonal antibody reactive with a flagellar protein of *P. aeruginosa*, an antimicrobial agent, a gamma globulin fraction from human blood plasma and a physiologically acceptable carrier (column 28, line 65-column 29, line 3). In contrast to the Examiner's statement, the composition of Claim 17 does not contain any immunogen.

Lenney *et al.* disclose experiments showing that Compound 48/80 has some antimicrobial activity. Lenney *et al.* are silent regarding immunogens, combining Compound 48/80 with other agents, or using Compound 48/80 to raise a therapeutic immune response in a subject.

Thus, neither Rosok *et al.* nor Lenney *et al.* disclose a method of inducing an immune response comprising administering an immunogen. Even when the teachings of Rosok *et al.* and Lenney *et al.* are combined, they fail to disclose every limitation of the presently claimed invention. Therefore, the present claims cannot be considered to be obvious over Rosok *et al.* in view of Lenney *et al.*

Applicants respectfully request that the rejection of claims 14 and 16-19 under 35 U.S.C. § 103(a) be withdrawn.

CONCLUSION

Accordingly, Applicant submits that the present application is in condition for allowance and the same is earnestly solicited. The Examiner is encouraged to telephone the undersigned at 919-854-1400 for resolution of any outstanding issues.

Respectfully submitted,

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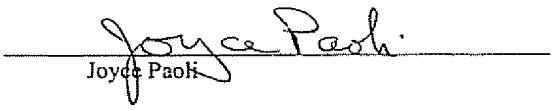
Signature: 
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